## REMARKS

Status of the Claims

Claims 1-18 are pending. Of these, claims 7-9 and 16-18 are withdrawn. Claims 1-6 and 10-15 are rejected. No claims are amended herein.

The 35 U.S.C. §102(b) Rejection

Claims 10-14 remain rejected under 35 U.S.C. §102(b) as being anticipated by **Chiesi** *et a* (WO 00/06132A2) as evidenced by **Basu** *et al* (U.S. 2002/0025348A1). Applicant respectfully traverses this rejection.

On page 3 of the Office Action mailed October 9, 2007, the Examiner cites **Chiesi** *et al* and **Basu** *et al* and compares it with the recitation of the instant claim 10. For instance, the Examiner states that **Chiesi** *et al* teach that pharmaceutical formulation for the treatment of inflammatory bowel disease containing beclomethasone dipropionate as an active ingredient. The Examiner also states that **Chiesi** *et al* teach that the formulation demonstrates no systemic absorption of beclomethasone dipropionate and its major active metabolites and also teach that the amount of beclomethasone dipropionate to be employed includes 3 mg and 5 mg. The Examiner states that **Basu** *et al.* report that irritable bowel syndrome (IBS) also tends to occur in inflammatory bowel disease patients who are in remission from the inflammatory bowel disease symptomologies.

Based on this, the Examiner concludes that inflammatory bowel disease patients disclosed by **Chiesi** *et al* are the patients in need of treatment of irritable bowel syndrome. Further, the Examiner states that the mechanism of action of increasing the threshold of pain to colorectal distention, thereby alleviating the symptoms of irritable bowel syndrome in the individual would be inherent in **Chiesi's** method of treating inflammatory bowel disease comprising identical patients having inflammatory bowel disease who are in need of alleviating the symptoms of irritable bowel syndrome as evidenced by **Basu** *et al*.

On pages 5-7 of the Office Action, the Examiner states that Applicant's arguments regarding the novelty of the treatments claimed are not persuasive since they involve the use of anti-inflammatory compounds in the treatment of a disorder that is not considered an inflammatory disorder and the difference in the histopathological changes in inflammatory bowel disease and IBS. The reason provided by the Examiner is that **Basu** *et al* teach that irritable bowel syndrome and inflammatory bowel disease are both inflammatory diseases that are treatable with agents that reduce inflammatory process. Based on this, the Examiner contends that although the histopathological changes are different in these disorders, it does not change the relevant teaching of **Basu** *et al* that irritable bowel syndrome and inflammatory bowel disease are inflammatory diseases that are treatable with anti-inflammatory agents that halt the inflammatory process.

Further, the Examiner states that Applicant's argument that utility of the method taught by **Chiesi** *et al* cannot be anticipated to alleviate the

symptoms of IBS based on the teachings of **Basu** *et al* unpersuasive. The reason provided by the Examiner is that **Chiesi** *et al* teach the same subject population required by claim 10. The Examiner is of the opinion that the inflammatory bowel disease patients disclosed by **Chiesi** *et al* are the individuals in need of treating symptoms of IBS as evidenced by **Basu** *et al* who teach that IBS tends to occur in inflammatory bowel disease patients. The Examiner states that **Basu** *et al* was used herein to show that inflammatory bowel disease patients are the individuals who are in need of treating symptoms of irritable bowel syndrome as irritable bowel syndrome tends to occur in inflammatory bowel disease patients. Based on this the Examiner contends that the claims are not patentably distinct over the cited prior art references.

Applicant respectfully disagrees with Examiner's contention that since **Basu** *et al* teach that irritable bowel syndrome tends to occur in IBD patients who are in remission from their IBD symptoms, the IBD patients disclosed by **Chiesi** *et al* are the patients that are in need of treatment of irritable bowel syndrome for the following reasons. There is a lot of discrepancy regarding the pathophysiology of irritable bowel syndrome in the art. The art, at present and at the time of filing of the instant invention treats irritable bowel syndrome and IBD as two distinct clinical syndromes. For instance, irritable bowel syndrome was and still is considered a functional bowel disorder and IBD is characterized by organic changes such as inflammation or ulceration in the small and/or large intestines. According to the symptom criteria (Rome criteria), once organic changes are detected, a diagnosis of functional disorder cannot be made. Thus, irritable bowel

syndrome and IBD are **distinct** disorders. Futhermore, Applicant had discussed the histopathological changes in irritable bowel syndrome and IBD in the previous response to show that although inflammation may be present in both, the inflammation in irritable bowel syndrome is different from the inflammation in IBD. This is discussed on page 13, line 15-page 14, line 5 of the instant specification. Applicant also encloses hard copy of the information regarding irritable bowel syndrome that is available on the NIH website(http://digestive.niddk.nih.gov/ddiseases/pubs/ibs/#what), which teaches that there is no link between irritable bowel syndrome and inflammatory bowel disease (see pgs. 5 and 6). Additionally, Applicant also provides another evidence published at the time of filing of the instant invention, which discloses that chronic inflammatory mucosal changes in the gut are not a plausible mechanism to explain the presence of chronic abdominal pain, which is a cardinal irritable bowel syndrome symptom (**Schwetz** *et al.*, Curr Gastroenterol Rep. 2003 Aug; 5(4): 331-336). Due to the non-specificity of the cardinal symptoms of abdominal pain or abdominal discomfort, the current diagnosis of irritable bowel syndrome applies to heterogenous group of patients. Therefore, given the state of art at the time of filing of the instant invention, one skilled in the art would not consider patients with IBD to be patients that need treatment for irritable bowel syndrome.

Additionally, **Chiesi** *et al* teach the use of topically active corticosteroid such as beclomethasone dipropionate in the treatment of inflammatory bowel disease such as Ulcerative colitis and Crohn's disease (pg.

1, lines 7-11). Neither **Chiesi** *et al* nor **Basu** *et al* or the combination thereof teach that administration of beclomethasone dipropionate or any other anti-inflammatory agent was effective in the alleviating the above-mentioned cardinal symptom of irritable bowel syndrome. Taken together, Applicant submits that alleviation of irritable bowel syndrome symptoms with an anti-inflammatory agent cannot be anticipated by the teachings of **Chiesi** *et al* as evidenced by **Basu** *et al*.

In distinct contrast, the instant claim 10 is drawn to a method of alleviating the symptoms of irritable bowel syndrome in an individual by adminstering pharmacologically effective amounts of active anti-inflammatory so as to increase the threshold of pain to colorectal distention. The example provided in the instant specification demonstrate the effectiveness of beclomethasone, an anti-inflammatory agent in increasing the threshold of pain to colorectal distention in rats that were sensitized with acetic acid. Hence, claim 10 is supported by the instant disclosure. Accordingly, based on the amendments and remarks presented herein, Applicant respectfully requests the withdrawal of rejection of claims 10-14 under 35 U.S.C. §102(b).

The 35 U.S.C. §103(a) Rejection

Claims 1-6 and 15 stand rejected under 35 U.S.C. §103(a) as being unpatentable over **Chiesi** *et al* (WO 00/06132A2) in view of **Basu** *et al* (U.S.2002/0025348A1). Applicant respectfully traverses this rejection.

On page 4 of the Office Action, the Examiner cites specific teachings of **Chiesi** *et al* and **Basu** *et al*. The teachings of **Chiesi** *et al* are the same as discussed supra. With regards to **Basu** *et al*., the Examiner states that they teach that the pathogenesis of inflammatory bowel disease and related disorders such as irritable bowel syndrome involve inflammation and that acute enteric inflammation is a symptom generated in irritable bowel syndrome. The Examiner states that this prior art reference teaches that reduction in inflammatory agents would significantly effect the treatment of inflammatory disease like irritable bowel syndrome and IBD. The Examiner further states that **Basu** *et al* teach that by treating inflammation, hyperalgesia potentated by the inflammatory factors would be prevented. The Examiner also states that **Basu** *et al* report that irritable bowel syndrome also tends to occur in IBD patients who are in remission from their IBD symptomologies.

Based on this, the Examiner contends that it would have been obvious to one of ordinary skill in the art to employ beclomethasone to an individual having irritable bowel syndrome for treatment of such disorder because beclomethasone is effective for the treatment of inflammatory bowel disorder related to inflammation and because irritable bowel syndrome is an inflammatory disorder taught by **Basu** *et al*. In addition to this, the Examiner states that one would have been motivated to make such modification in order to achieve an expected anti-inflammatory effect of beclomethasone to halt inflammation process generated as a symptom of irritable bowel syndrome. Further, the Examiner points out that the 5mg amount employed by **Chiesi** *et al* is within the mg/kg recited in claims 6 and 15, when the subject to be treated weighed 50kg. Based on all of this

and the reasons provided by the Examiner for finding Applicant's previous arguments unpersuasive (see supra), the Examiner maintains that the claims fail to patentably distinguish over the state of art represented by the cited references. Applicant respectfully disagrees with the Examiner.

The teachings of the instant invention are as discussed supra. These teachings support the recitations of the instant claims. As discussed supra, there is a lot of discrepancy in the art regarding the pathophysiology of irritable bowel syndrome. Pages 5-6 of the hardcopy of the information on NIH website enclosed along with this response provides evidence that irritable bowel syndrome and IBD are not linked. In fact, **Basu** *et al* state that there is no satisfactory explanation regarding the pathophysiology of irritable bowel syndrome. IBD is characterized by organic changes such as inflammation and/or ulceration in the small and/or large intestines and IBS is characterized as a functional disorder. According to the symptom criteria (Rome criteria), once organic changes are detected, a diagnosis of functional disorder cannot be made. Thus, irritable bowel syndrome and IBD are **distinct** disorders. Furthermore, due to the non-specificity of the cardinal symptoms of abdominal pain or abdominal discomfort, the current diagnosis of irritable bowel syndrome applies to heterogenous group of patients.

Applicant respectfully points to page 3 of the NIH disclosure that states that bleeding, fever, weight loss and persistent severe pain are **not** symptoms of IBS and may indicate other problems such as inflammation or rarely, cancer. In other words, one cannot categorize IBS to be an inflammatory

disorder. This also contradicts Examiner's statement of IBS and IBD being inflammatory diseases on page 6 of the Office Action. Additionally, the Examiner's statement that IBS tends to occur in IBD patients who are in remission from their IBD symptomologies also would lead one not to speculate that inflammation is involved in the occurrence of IBS because if the inflammation persisted, then the patient would still be diagnosed as having IBD and not IBS. Furthermore, the last paragraph on pg. 13 of the instant specification discusses how the inflammation if present, in IBS is different from IBD and may involve mechanisms that are different from IBD in contributing to the pathogenesis of IBS. Applicant also provides a report that was published at the time of filing of the instant invention, which teaches that chronic inflammatory mucosal changes in the gut are not plausible mechanism to explain the presence of chronic abdominal pain, a cardinal IBS symptom (**Schwetz** *et al.*, Curr Gastroenterol Rep. 2003 Aug; 5(4): 331-336). Hence, one of skill in the art would not be motivated to use an anti-inflammatory agent to treat IBS.

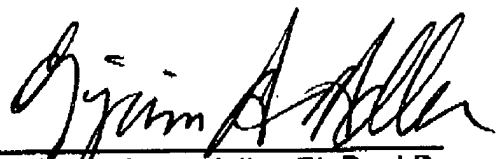
Furthermore, even if one of skill in the art were motivated to use an anti-inflammatory agent based on teachings of **Basu** *et al.*, there would be no reasonable expectation in treating IBS based on the report discussed supra and since neither **Chiesi** *et al* nor **Basu** *et al* actually demonstrate that the anti-inflammatory agent actually was successful in treating IBS or the symptoms of IBS discussed herein. Taken together, Applicant submits that the instant claims are not prima facie obvious over the teachings of prior art references.

Accordingly, based on the above-mentioned remarks, Applicant respectfully requests the withdrawal of rejection of claims 1-6 and 15 under 35 U.S.C. §103(a).

This is intended to be a complete response to the Final Office Action mailed October 9, 2007. Applicants also enclose a Petition for Extension of Time and PTO Form- 2038 along with the response. Applicant submits that the pending claims are in condition for allowance. If any issues remain outstanding, please telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

Date: Feb 8, 2008



Benjamin Aaron Adler, Ph.D., J.D.
Registration No. 35,423
Counsel for Applicant

ADLER & ASSOCIATES
8011 Candle Lane
Houston, Texas 77071
(713) 270-5391 (tel.)
(713) 270-5361 (fax.)
BEN@adlerandassociates.com